

REMARKS

Claims 1-14 and 44-45 were rejected by the Office Action. Claims 15-43 were previously cancelled. Claim 1 has been amended. Claim 4 has been canceled as the claimed limitations have been incorporated into claim 1. No new matter has been added by these amendments.

Interview Summaries

On August 5, 2010, a telephone interview took place between Mr. Gary Connell (Applicants' Representative), Dr. Angela Domitrovich (Applicants' Representative) and Examiner Davis. Applicants thank the Examiner for the courtesy extended during the interview. During this interview, Applicants' Representatives discussed that the Radin prior art reference teaches the use of biologically active molecules as a coating and that a skilled person would understand from Radin, that if such coatings were to be used, they would be in small amounts well outside of the claimed range of 5% to 95% by volume. Moreover, Applicants' Representatives stated that cancellous bone and DBM are not within the meaning of the biological active molecules of the cited prior art as they are not coatings. No agreement with respect to the claims was reached during this interview.

On August 23, 2010, a telephone interview took place between Mr. Connell, Dr. Domitrovich and Examiner Davis. Applicants thank the Examiner for the courtesy extended during the interview. During this interview, Applicant's Representative proposed claim amendments to further distinguish the claimed invention over the prior art, specifically the amount of bone graft material. The Examiner at this time agreed to reconsider the rejection with the submission of claim amendments and support. No agreement with respect to the claims was reached during this interview.

Rejection Under 35 USC §103(a) Radin in view of Walter et al., or Jeffries and further in view of Lemons

The Examiner has rejected Claims 1-6 and 44-45 under 35 USC § 103(a) as being unpatentable over Radin (CA 2253649), in view of Walter et al., (U.S. Patent No. 5716413) (herein referred to as "Walter") or Jeffries (U.S. Patent No. 4472840) and further in view of

Lemons (U.S. Patent No. 5237964). To establish a *prima facie* case of obviousness under 35 U.S.C. 103(a), the Examiner must show that (1) the references teach all the elements of the claimed invention, (2) the references contain some teaching, suggestion or motivation to combine the references, and (3) the references suggest a reasonable expectation of success.

The Office action states that "Radin teaches compositions comprising hollow calcium phosphate containing glass shells (abstract) that are combined with biologically active molecules effective to repair bony defects (p.8)." The Office action further states that "Radin does not teach compositions wherein the biologically active molecule is cancellous bone or DBM." The Office action uses the teachings of Walter (stating that Walter teaches cancellous bone is used for filling or repairing bone defects) and Jefferies (stating that Jefferies teaches DBM is useful for repairing bony defects) to conclude that it would be obvious to one of skill in the art to substitute DBM or cancellous bone as the biologically active molecules disclosed in Radin.

Applicants respectfully disagree with this conclusion and maintain that the biologically active molecules of Radin are not in any way equivalent to the bone graft material of the current claims. Solely in the interest of expediting prosecution, Applicants have amended Claim 1 to further define the bone grafting composition of the present invention by specifying that the bone graft material is from about 5% to about 95% by volume of the composition. The cited combination of references do not meet, *inter alia*, the claim limitation of a bone graft material (cancellous bone, de-mineralized bone matrix and mixtures thereof) being from about 5% to about 95% by volume of the composition. Radin discloses the use of biologically active molecules to "coat" hollow particles (p.7 ll. 24-32). Radin does not explicitly disclose a quantity of such biologically active molecules. The only quantitative example of the incorporation of a biologically active molecule in Radin is found in Example 1 of Radin which discloses the use of 1.2 mg of the antibiotic vancomycin per gram of silica (i.e. at a level of 0.12%). Therefore a skilled person would understand the amount of biologically active molecule in a coating to be significantly less than the claimed range of about 5% to about 95%. It is well known in the art that when biologically active molecules (as used in Radin, such as growth factors, cytokines, antibiotics, anti-inflammatory agents, analgesics, and cell attachment molecules) are used as a coating, they are presented in

amounts significantly less than 5%. Submitted herewith is a Declaration submitted in accordance with 37 C.F.R. § 1.132 from the Dr. Keyvan Behnam, a skilled person in the field of bone grafts which supports the statements made above. Courtesy copies of the references discussed in this Declaration are also being submitted herewith. Dr. Behnam concludes that a skilled person reviewing the disclosure of Radin would understand the disclosure of a coating of a biologically active molecule to refer to an amount significantly less than 5% by volume. This conclusion is based at least in part on the disclosure in Radin, Example 1, that the biologically active molecule vancomycin is present at a level of 0.12%. In addition, the references cited in the Declaration disclose the use of coatings of biologically active molecules in bone applications in amounts of 0.0067%, 0.2% and 0.043%.

In addition, Radin's disclosed processes for coating microstructures require that the "biologically active molecules" be soluble. The immersion coating process defined in Radin (p. 7, ll. 33-37) relies on allowing a soluble biological molecule to either incorporate into the calcium phosphate layer or attach to the surface. The claimed bone graft materials of cancellous bone and de-mineralized bone matrix (DBM) are insoluble, further supporting that the biologically active molecules of Radin are not in any way equivalent to the bone graft material of the current claims.

Thus, the Examiner's position that it would have been obvious to substitute the bone graft material of the present invention for the biologically active molecules of Radin is incorrect. As previously discussed, Radin teaches the use of hollow particles as a bone graft material, and not the use of either cancellous bone or DBM as a bone graft material. In addition, as described above Radin does not teach or suggest the claim limitation of a bone graft material being from about 5% to about 95% by volume of the composition. Accordingly, the Examiner has not established a *prima facie* case of obviousness.

The Office action goes on to point out that Radin does not teach microstructures comprising each of the claimed materials and takes the position that it would have been obvious to use any of the claimed materials since they were routinely used in such compositions. Lemons is used to support this assumption stating that Lemons teaches a composition comprising calcium particles made from sintered tricalcium phosphate and/or hydroxylapatite. However, Lemons does not make up for the deficiencies of Radin, Walter

and Jefferies as described above and thus no *prima facie* case of obviousness has been established.

Based on the foregoing discussion, and the accompanying Declaration, the Applicants contend that neither Radin, Walter, Jefferies and Lemons, whether alone or in combination, can be used to render Claims 1-6 and 44-45, obvious. Reconsideration and withdrawal of this rejection is respectfully requested.

Rejection Under 35 USC §103(a) Radin in view of Walter et al., or Jeffries and further in view of Gerhart

The Examiner has rejected Claims 1-3, 7-14 and 44-45 under 35 USC § 103(a) as being unpatentable over Radin (CA 2253649), in view of Walter et al., (herein referred to as “Walter”) (U.S. Patent No. 5716413) or Jeffries (U.S. Patent No. 4472840) and further in view of Gerhart (U.S. Patent No. 5085861). The Office action uses the teaching of Radin, Walter and Jeffries as above and further states that “Radin does not teach the composition further comprising a bonding agent that is one of the claimed polymers or calcium containing cements”. Applicants believe that the Examiner inadvertently included claims 1-3 in this rejection, as claims 1-3 do not include the additional limitation of bonding agents such as cements or polymers. The Examiner asserts that “Gerhart teaches that cements are well known and commonly used in compositions for repairing and fixing bone defects” and that one of skill in the art would have been motivated by the teachings of Gerhart to include the claimed cements or polymers as a bonding agent in the composition of Radin. In this rejection, the combination of references fails to teach all of the elements of the claimed invention. Gerhart does not make up for the deficiencies of Radin, Walter or Jeffries as discussed above. Gerhart does not disclose hollow microstructures. Since Gerhart does not make up for the deficiencies of Radin, Walter or Jeffries, no *prima facie* case of obviousness has been established and withdrawal of this rejection is respectfully requested.

In view of the foregoing amendments, Applicants submit that the current claims are allowable and favorable consideration of the same is hereby requested.

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Respectfully submitted,

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